

Application No. 10/821,726

Attorney Docket No. 023004.0104N4US

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AMENDMENTS TO THE CLAIMS

1.-33. (Canceled)

34. (Currently Amended) A method for producing an RNA molecule which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal isolated eukaryotic cell comprising introducing ~~an RNA nucleic acid molecule to in the cell, wherein the RNA nucleic acid molecule includes a~~ is produced by transcription product of into an isolated eukaryotic cell a synthetic genetic construct comprising a mammalian terminator and at least two copies of a structural gene sequence operably under the control of a single promoter and a terminator sequence which contains a polyadenylation signal and is active in the cell, wherein said structural gene sequence comprises a nucleotide sequence which is at least 80% identical to at least a region a sequence of 30 contiguous nucleotides of said target gene, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation and wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of the promoter; wherein said two copies of said structural gene sequence are spatially separated by a stuffer fragment which comprises a sequence of nucleotides, and wherein the synthetic genetic construct is transcribed to produce the RNA molecule.

35.-87. (Canceled)

88. (New) The method of claim 34, wherein the target gene is a viral gene.

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89. (New) The method of claim 34, wherein the cell is a plant cell.
90. (New) The method of claim 89, wherein the target gene is a viral gene.
91. (New) The method of claim 88, wherein the viral gene encodes a DNA polymerase, RNA polymerase or viral coat protein.
92. (New) The method of claim 34, wherein the target gene is from a lentivirus.
93. (New) The method of claim 34, wherein the target gene is from an immuno deficiency virus.
94. (New) The method of claim 34, wherein the target gene is from a single-stranded (+) RNA virus.
95. (New) The method of claim 34, wherein the target gene is from a double-stranded DNA virus.
96. (New) The method of claim 34, wherein the target gene is a transgene in the cell.
97. (New) the method of claim 34, wherein the target gene is an endogenous gene of the cell.
98. (New) The method of claim 97, wherein the cell is a plant cell.

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99. (New) The method of claim 97, wherein the cell is an animal cell.

100. (New) The method of claim 34, wherein the contiguous nucleotides of the target gene corresponds to a coding region of the target gene.

101. (New) The method of claim 34, wherein the 30 contiguous nucleotides of the target gene corresponds to a 5' or 3' – untranslated sequence of the target gene.

102. (New) The method of claim 34, wherein the transcribed region of the genetic construct comprises an intron.

103. (New) The method of claim 34, wherein the stuffer fragment is a sequence of nucleotides 10-50 nucleotides in length, 50-100 nucleotides in length, or 100-500 nucleotides in length.

104. (New) The method of claim 34, wherein the stuffer fragment comprises an intron.

105. (New) The method of claim 34, wherein the total length of said structural gene sequences is no more than 2.0 kilobases.

106. (New) The method of claim 34, wherein the total length of said structural gene sequences is no more than 0.5 kilobases.

107. (New) The method of claim 34, wherein the two copies are in a head-to-head orientation relative to each other.

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108. (New) The method of claim 34, wherein the two copies are in a tail-to-tail orientation relative to each other.

109. (New) The method of claim 34, comprising transfecting the cell with the genetic construct.

110. (New) The method of claim 34, wherein the genetic construct is delivered to the cell in a virus particle.

111. (New) The method of claim 34, wherein the genetic construct is delivered to the cell in a liposome.

112. (New) The method of claim 34, wherein the genetic construct is integrated into the genome of the cell.

113. (New) The method of claim 34, wherein the genetic construct has only two copies of said structural gene sequence.

114. (New) A method for producing an RNA molecule which is capable of delaying, repressing or otherwise reducing the expression of a target gene in a plant cell comprising introducing into the plant cell a synthetic genetic construct comprising two copies of a structural gene sequence operably under the control of a single promoter and a terminator sequence which contains a polyadenylation signal and is active in the cell, wherein said structural gene sequence comprises a nucleotide sequence which is identical to a sequence of 30 contiguous nucleotides of said

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target gene, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation and at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of the promoter; wherein said two copies of said structural gene sequence are spatially separated by a stuffer fragment which comprises a sequence of nucleotides, and wherein the synthetic genetic construct is transcribed to produce the RNA molecule.

115. (New) The method of claim 114, wherein the target gene is a viral gene.

116. (New) The method of claim 115, wherein the viral gene encodes a DNA polymerase, RNA polymerase or viral coat protein

117. (New) The method of claim 11, wherein the target gene is from a single-stranded (+) RNA virus.

118. (New) The method of claim 11, wherein the target gene is from a double-stranded DNA virus.

119. (New) The method of claim 11, wherein the target gene is a transgene in the cell.

120. (New) The method of claim 11, wherein the target gene is an endogenous gene of the cell.

121. (New) The method of claim 11, wherein the 30 contiguous nucleotides of the target gene corresponds to a coding region of the target gene.

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122. (New) The method of claim 11, wherein the 30 contiguous nucleotides of the target gene corresponds to a 5'- or 3'- untranslated sequence of the target gene.

123. (New) The method of claim 11, wherein the transcribed region of the genetic construct comprises an intron.

124. (New) The method of claim 11, wherein the stuffer fragment is a sequence of nucleotides 10-50 nucleotides in length, 50-100 nucleotides in length, or 100-500 nucleotides in length.

125. (New) The method of claim 114, wherein the stuffer fragment comprises an intron.

126. (New) The method of claim 11, wherein the total length of said structural gene sequences is no more than 2.0 kilobases.

127. (New) The method of claim 126, wherein the total length of said structural gene sequences is no more than 0.5 kilobases.

128. (New) The method of claim 11, wherein the two copies are in a head-to-head orientation relative to each other.

129. (New) The method of claim 11, wherein the two copies are in a tail-to-tail orientation relative to each other.

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130. (New) The method of claim 11, wherein the genetic construct is integrated into the genome of the cell.

131. (New) The method of claim 11, wherein the genetic construct has only two copies of said structural gene sequence.

132. (New) The method of claim 114, wherein the cell is comprised in a transgenic plant.

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